REMARKS/ARGUMENTS

Claims 28, 29, 33, and 36 are pending in the application and have been rejected. Newly presented claims 37-40 are added.

Rejection under 35 USC §112

Claims 33, 28, 29 and 36 were rejected under 35 USC 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention.

In particular, the Examiner avers that claims 33 and 36 are indefinite over the recitation of the limitations ". . . first and second nucleic acid sequences . . . which are separated from each other along said opposing strands by from 90 to 400 nucleotides . . ." and " . . . third and fourth nucleic acid sequences and being different from said first and second nucleic acid sequences and being separated from each other along said opposing strands . . . by from 90 to 400 nucleotides . . . (emphasis is Examiner's). The Examiner avers it is not clear how the separation of the first and second, or third and fourth nucleic acid sequences is determined; these sequences are complementary to first and second, or third and fourth, respectively, primer sequences; a primer has a 5' end, N nucleotides and a 3' end. Therefore a distance between two primer-complementary sequences can be measured, for example, either between the 5' ends of the first and second primer (Or third and fourth primer) or between the 3' ends of the first and second primer (or third and fourth primer); that in the first case the separation between the first and second sequences would be larger from the separation obtained in the second case by the sum of nucleotides present in each primer; that for example, if 5'-5'

separation is 400 bp, and each primer has 20 bp, the 3'-3' separation would be 360 bp.

Applicants have considered the Examiner's comments and have amended independent claims 33 and 36 to recite that " . . . first and second nucleic acid sequences which are in opposing strands of a first target DNA and which are separated from each other along said opposing strands by from 90 to 400 nucleotides as measured as 5' to 5' . . .", and have added new, identical claims 37 and 40 that recite wherein measurement is 3' to 3'. It is respectfully submitted that such is within the scope of Applicants' teaching while satisfying the requirement of particularly pointing out and claiming Applicants' invention. Applicants respectfully request this rejection be withdrawn.

Rejection under 35 U.S.C. §102

Claim 36 was rejected under 35 USC §102(b) as being anticipated by Frank et al. It is averred that Frank et al. teach simultaneous amplification and simultaneous detection of three different target nucleic acids using three different primer pairs; the target nucleic acid are CMV MIE gene, CMV LA gene and human beta-hemoglobin gene; that primers used for amplification of these sequences are listed in Table 1; that only primers used in the first round of amplification were considered with respect to their length, melting temperature and length of amplification product (which corresponds to 5'-5' end separation of primers). The Examiner next avers that the

primer melting temperatures were calculated using (Applicants') formula (I) given on page 12, line 30, and supplies the calculations for the various primers used by Frank et al.

The Examiner thus concludes that the primer sets for CMV LA and hemoglobin satisfy the requirements of having melting temperatures within 2 degrees of each other, the lengths of each pair of primers within 5 bp of each other and their separation (as measured by the amplification product size) within the range of 90-400 bp.

The Examiner next avers that Frank et al. each using these primers in a PCR reaction which contained 200 uM of each dNTP, 10% of 10x Taq DNA polymerase buffer (from Promega) and 5 units Taq polymerase; that the PCR reaction parameters for the first round included 2 minutes at 64 degrees C for primer annealing and 2 minutes at 72 degrees C for primer extension (page 450 para 3 and 4); the amplification products were simultaneously detected by electrophoresis on a 3% NuSieve/1% agarose gel containing 0.5 ug/mL ethidium bromide. While the Examiner admits that Frank et al. do not explicitly teach Taq DNA polymerase cofactor Mg^{2+} or Mn^{2+}, Frank et al. teach using 10X Taq polymerase buffer from Promega, and as evidenced by 1992-93 Promega catalog, 10X polymerase buffer contained $MgCl_2$.

Applicants traverse this rejection for the following reasons.

Applicants' claim 36 requires that the primer melting temperatures (in degrees C) be within about 2 degrees of each other. Applicants performed the calculations presented by the Examiner and respectfully submit that there is an error in the Examiner's calculation of the Hb 3' primer. The melting temperature should be 68.1 degrees and not 69.5 degrees as suggested by the Examiner. Thus, the Hb and CMV LA primers span more than 2 degrees C melting temperature, therefore not falling within Applicants' claim.

Applicants question the Examiner's suggestion that in Frank et al. "Primer melting temperatures were calculated using formula (I) given on page 12, line 30", the latter referring to Applicants' formula. Applicants respectfully point out that this formula was determined empirically, and first disclosed in the parent application hereto filed May 14, 1993. Since Frank et al. was published in 1992 the authors could not have used Applicants' formula.

Finally, Frank et al. at page 452, paragraph bridging center column to top of right hand column, state that they more efficiently amplified the LA product than the MIE, with the MIE product in some cases being absent altogether. The authors suggest that this effect in their multiplex reaction is due to competition for Taq polymerase by the smaller more efficiently amplified LA-derived PCR product. Applicants, on the other hand, were able to efficiently amplify all products. See Figures 1-9.

For all the above reasons, Applicants respectfully submit that nothing in Frank et al. teaches or suggests Applicants' invention as claimed, and that this rejection should respectfully be withdrawn.

Double Patenting

Claims 33 and 36 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14 and 2, respectively, of U.S. Patent No. 6,174,668 in view of Tavernarakis et al. (US Patent No. 5,569,582). As was previously suggested by the Examiner, Applicants herein present a timely-filed terminal disclaimer under 37 CFR 1.321(c) to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with the subject application, referring to 37 CFR 1.130(b). Applicants herein state that U.S. Patent No. 6,174,668 is commonly owned with the subject application, and herein file the required terminal disclaimer.

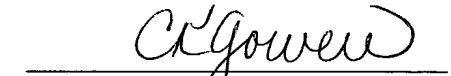
The Examiner states that no references were found teaching or anticipating claims 33, 28 and 29, but that they were rejected for other reasons given earlier in the Office Action. Applicants respectfully submit that the other reasons are (1) 35 USC 112 matters, which the amendment to claim 33 has, in Applicants' opinion, fully addressed, and (2) the request for a terminal disclaimer which Applicants have herewith submitted. Therefore, Applicants respectfully submit that all of claims 33, 28, 29 and 36, as well as newly presented claims 37-40, are

patentable. Entry of these amendments and allowance of the application on the merits is earnestly solicited.

If a telephone interview would be of assistance in advancing prosecution of the subject application, the Examiner is invited to telephone Applicants' undersigned attorney at the number provided.

If any fees are due in connection with the filing of this amendment, authorization is hereby granted to charge the amount of such fee to Deposit Account No.10-0750/CDS-226/CKG in the name of Johnson & Johnson.

Respectfully submitted,



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